

# MEDICAL POLICY

<b>POLICY TITLE</b>	<b>HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY FOR SELECT INTRA-ABDOMINAL AND PELVIC MALIGNANCIES</b>
<b>POLICY NUMBER</b>	<b>MP-2.021</b>

<b>Effective Date:</b>	<b>1/1/2024</b>
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## I. POLICY

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Cytoreductive surgery (CRS) plus hyperthermic intraperitoneal chemotherapy (HIPEC) may be considered **medically necessary** for the treatment of:

- Pseudomyxoma peritonei; **AND**
- Diffuse malignant peritoneal mesothelioma

The use of HIPEC may be considered **medically necessary** in newly diagnosed epithelial ovarian or fallopian tube cancer at the time of interval cytoreductive surgery when **ALL** of the following criteria are met:

- The individual has stage III disease (see Policy Guidelines);
- The individual is not eligible for primary cytoreductive surgery or surgery had been performed but was incomplete and will receive neoadjuvant chemotherapy and subsequent interval debulking surgery (see Policy Guidelines); **AND**
- It is expected that complete or optimal cytoreduction can be achieved at time of the interval debulking surgery (see Policy Guidelines).

The use of HIPEC in all other settings to treat ovarian cancer, including but not limited to stage IIIC or IV ovarian cancer, is considered **investigational**.

Cytoreductive surgery plus HIPEC are considered **investigational** for:

- Peritoneal carcinomatosis from colorectal cancer, gastric cancer, or endometrial cancer; **AND**
- All other indications, including goblet cell tumors of the appendix.

There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with these procedures.

The National Comprehensive Cancer Network (NCCN) is a nonprofit alliance of cancer centers throughout the United States. NCCN develops the Clinical Practice Guidelines in Oncology which are recommendations aimed to help health care professionals diagnose, treat, and manage patients with cancer. The National Cancer Institute's PDQ (Physician Data Query) is NCI's comprehensive source of cancer information, which includes evidence-based summaries on topics that cover adult and pediatric cancer treatment. These guidelines evolve continuously

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as new treatments and diagnostics emerge and may be used by Capital Blue Cross when determining medical necessity according to this policy.

### Policy Guidelines

Ovarian cancer staging is as follows:

- Stage I: The cancer is confined to the ovary or fallopian tube.
- Stage II: The cancer involves one or both ovaries with pelvic extension.
- Stage III: The cancer has spread within the abdomen.
- Stage IV: The cancer is widely spread throughout the body.

Eligibility for neoadjuvant chemotherapy and interval debulking surgery is based on a high perioperative risk profile (i.e., the patient is a poor candidate to withstand an aggressive initial cytoreductive procedure) or a low likelihood of achieving cytoreduction to less than 1 cm (i.e., the patient has extensive disease that precludes upfront optimal cytoreduction) or surgery has been performed but was incomplete (i.e., after surgery, one or more residual tumors measuring greater than 1 cm in diameter were present).

Complete cytoreduction is defined as no visible disease and optimal cytoreduction as one or more residual tumors measuring 10 mm or less in diameter remaining.

## II. PRODUCT VARIATIONS

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This policy is only applicable to certain programs and products administered by Capital BlueCross and subject to benefit variations as discussed in Section VI. Please see additional information below.

**FEP PPO** - Refer to FEP Medical Policy Manual. The FEP Medical Policy manual can be found at:

<https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies>.

## III. DESCRIPTION/BACKGROUND

Cytoreductive surgery (CRS) includes peritonectomy (ie, peritoneal stripping) procedures and multivisceral resections, depending on the extent of intra-abdominal tumor dissemination. Cytoreductive surgery may be followed by infusion of intraperitoneal chemotherapy with or without heating, which is intended to improve the tissue penetration of the chemotherapy. When heated, this is referred to as hyperthermic intraperitoneal chemotherapy (HIPEC). Cytoreductive surgery and HIPEC have been proposed for a number of intra-abdominal and pelvic malignancies such as pseudomyxoma peritonei and peritoneal carcinomatosis from colorectal, gastric, or endometrial cancer.

### Pseudomyxoma Peritonei

Pseudomyxoma peritonei is a clinicopathologic disease characterized by the production of mucinous ascites and mostly originates from epithelial neoplasms of the appendix. Appendix

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cancer is diagnosed in fewer than 1000 Americans each year; less than half are epithelial neoplasms. The incidence of pseudomyxoma peritonei is estimated at 2 cases per 1 million individuals. As mucin-producing cells of the tumor proliferate, the narrow lumen of the appendix becomes obstructed and subsequently leads to appendiceal perforation. Neoplastic cells progressively colonize the peritoneal cavity and produce copious mucin, which collects in the peritoneal cavity. Pseudomyxoma peritonei ranges from benign (disseminated peritoneal adenomucinosis) to malignant (peritoneal mucinous carcinomatosis), with some intermediate pathologic grades. Clinically, this syndrome ranges from early pseudomyxoma peritonei, usually discovered during imaging or laparotomy performed for another reason, to advanced cases with a distended abdomen, bowel obstruction, and starvation.

**Treatment**

The conventional treatment of pseudomyxoma peritonei is surgical debulking, repeated as necessary to alleviate pressure effects. However, repeated debulking surgeries become more difficult due to progressively thickened intra-abdominal adhesions, and this treatment is palliative, leaving visible or occult disease in the peritoneal cavity.

**Peritoneal Carcinomatosis of Colorectal Origin**

Peritoneal dissemination develops in 10% to 15% of patients with colon cancer.

**Treatment**

Despite the use of increasingly effective regimens of chemotherapy and biologic agents to treat advanced disease, peritoneal metastases are associated with a median survival of 6 to 7 months.

**Peritoneal Carcinomatosis of Gastric Origin**

Peritoneal carcinomatosis is detected in more than 30% of patients with advanced gastric cancer and is a poor prognostic indicator. The median survival is 3 months, and 5-year survival is less than 1%. Sixty percent of deaths from gastric cancer are attributed to peritoneal carcinomatosis.

**Treatment**

Current chemotherapy regimens are nonstandard, and peritoneal seeding is considered unresectable for cure.

**Peritoneal Mesothelioma**

Malignant mesothelioma is a relatively uncommon malignancy that may arise from the mesothelial cells lining the pleura, peritoneum, pericardium, and tunica vaginalis testis. In the United States, 200 to 400 new cases of diffuse malignant peritoneal mesothelioma are registered every year, accounting for 10% to 30% of all-type mesothelioma. Diffuse malignant peritoneal mesothelioma has traditionally been considered a rapidly lethal malignancy with limited and ineffective therapeutic options. The disease is usually diagnosed at an advanced stage and is characterized by multiple variably sized nodules throughout the abdominal cavity. As the disease progresses, the nodules become confluent to form plaques, masses, or uniformly cover peritoneal surfaces. In most patients, death eventually results from locoregional

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progression within the abdominal cavity. In historical case series, treatment by palliative surgery, systemic or intraperitoneal chemotherapy, and abdominal irradiation has resulted in a median survival of 12 months.

### **Treatment**

Surgical cytoreduction (resection of visible disease) in conjunction with hyperthermic intraperitoneal chemotherapy (HIPEC) is designed to remove visible tumor deposits and residual microscopic disease. By delivering chemotherapy intraperitoneally, drug exposure to the peritoneal surface is increased some 20-fold compared with systemic exposure. In addition, previous animal and in vitro studies have suggested that the cytotoxicity of mitomycin C is enhanced at temperatures greater than 39°C (102.2°F).

### **Ovarian Cancer**

Several different types of malignancies can arise in the ovaries; epithelial carcinoma is the most common, accounting for 90% of malignant ovarian tumors. Epithelial ovarian cancer is the fifth most common cause of cancer death in women in the United States. Most ovarian cancer patients (greater than 70%) present with widespread disease, and annual mortality is 65% of the incidence rate. In addition, African American women reportedly have a higher prevalence of presenting with more advanced tumors, being undertreated or untreated, and having shorter disease-free survival compared to other racial groups.

### **Treatment**

Current management of advanced epithelial ovarian cancer is cytoreductive surgery (CRS) followed by combination chemotherapy. Tumor recurrences are common, and the prognosis for recurrent disease is poor.

CRS plus HIPEC in combination with systemic chemotherapy is being studied for primary and recurrent disease. Because HIPEC is administered at the time of surgery, treatment-related morbidity may be reduced compared with intraperitoneal chemotherapy administered postoperatively.

### **Regulatory Status**

Mitomycin, oxaliplatin, carboplatin, and other drugs used for HIPEC have not been approved by the U.S. Food and Drug Administration (FDA) for this indication.

Several peritoneal lavage systems (FDA product code: LGZ) have been cleared for marketing by the FDA through the 510(k) process to provide “warmed, physiologically compatible sterile solution” (e.g., Performer® HT perfusion system; RanD). None has received marketing approval or clearance to administer chemotherapy. The FDA has issued warnings to manufacturers of devices that are FDA-cleared for peritoneal lavage using sterile saline solutions when these devices are marketed for off-label use in HIPEC.

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**Table 1. Hyperthermic Intraperitoneal Lavage Devices Cleared by the U.S. Food and Drug Administration**

<b>Device</b>	<b>Manufacturer</b>	<b>Date Cleared</b>	<b>510(k) No.</b>	<b>Indication</b>
<b>FluidSmart</b>	THERMEDX LLC	9/5/2017	K172048	For irrigation, distention, fluid warming, and fluid volume/deficit measurements in endoscopic procedures within gynecology, urology, and orthopedic disciplines.
<b>Hang&amp;Go PAC</b>	RanD S.r.l.	12/28/2016	K161613	To recirculate, filtrate and perfuse physiologically compatible sterile solution (i.e., saline solution) in the thoracic or abdominal cavity
<b>The Belmont Hyperthermia Pump</b>	BELMONT INSTRUMENT CORPORATION	9/2/2015	K152208	To raise the temperature of the thoracic or peritoneal cavity to the desired target temperature by continuously lavaging the cavity with circulating warmed sterile solution

#### IV. RATIONALE

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##### **Summary of Evidence**

For individuals who have pseudomyxoma peritonei who receive CRS plus HIPEC, the evidence includes cohort studies and a systematic review. Relevant outcomes are overall survival (OS), disease-specific survival, quality of life (QOL), and treatment-related mortality and morbidity. Retrospective cohort studies and systematic reviews have reported median survival ranging from 47 to 156 months and 5-year OS ranging from 41% to 96% for patients with primary treatment for pseudomyxoma peritonei treated with CRS plus HIPEC. Two retrospective studies reported results of CRS plus HIPEC for recurrence with 5-year OS rates of 34% and 79%. Although no direct comparisons between CRS plus HIPEC and other interventions have been

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published, traditional surgical debulking is not curative, and complete CRS alone (without HIPEC) has been associated with a 5-year OS of approximately 50%, along with high recurrence rates (91%, with a median disease-free survival of 24 months). Median progression-free survival (PFS) with CRS plus HIPEC as primary treatment has been reported as 40 to 78 months, with 5-year PFS rates of 38% to 80%. Procedure-related morbidity and mortality have generally decreased over time. Because the prevalence of pseudomyxoma peritonei is very low, conducting comparative trials is difficult. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have peritoneal carcinomatosis of colorectal origin who receive CRS plus HIPEC, the evidence includes RCTs, systematic reviews, and a large number of observational studies. Relevant outcomes are OS, disease-specific survival, QOL, and treatment-related mortality and morbidity. A meta-analysis of controlled studies found that CRS plus HIPEC, compared with traditional therapy without HIPEC, was associated with significantly higher survival rates and was not associated with significantly higher treatment-related morbidity rates. One RCT, in which patients with peritoneal carcinomatosis due to colorectal cancer were followed for at least 6 years, demonstrated improved survival in patients who received CRS plus HIPEC, and systemic chemotherapy compared with patients who received systemic chemotherapy alone. However, procedure-related morbidity and mortality rates were relatively high, and systemic chemotherapy regimens did not use currently available biologic agents. A more recent RCT found no survival benefit with CRS plus HIPEC over CRS alone, and a higher rate of adverse events 31 to 60 days post-procedure in the CRS plus HIPEC group. The lack of benefit seen with HIPEC in this trial may have been due to several factors, including the short duration of HIPEC treatment, the extensive use of preprocedural systemic chemotherapy, and the high rates of complete cytoreduction achieved in both groups. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have peritoneal carcinomatosis of gastric origin who receive CRS plus HIPEC, the evidence includes 2 small RCTs, observational studies, and 2 systematic reviews. Relevant outcomes are OS, disease-specific survival, QOL, and treatment-related mortality and morbidity. A 2017 meta-analysis identified 2 RCTs and 12 controlled nonrandomized studies comparing surgery plus HIPEC with standard surgical management in patients who had peritoneal carcinomatosis due to gastric cancer. One meta-analysis found significantly better survival in the surgery plus HIPEC group at 1 year but not at 2 or 3 years. Another meta-analysis found survival benefit was reported in the CRS plus HIPEC groups at 1,2 and 3 years. One small (N=17) preliminary RCT showed improved survival in patients with peritoneal carcinomatosis due to gastric cancer who received CRS plus HIPEC compared with patients who received chemotherapy alone. Another (N=68) RCT showed improved survival in patients who received CRS plus HIPEC compared with CRS alone. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have peritoneal carcinomatosis of endometrial origin who receive CRS plus HIPEC, the evidence includes cohort studies. Relevant outcomes are OS, disease-specific survival, QOL, and treatment-related mortality and morbidity. Only uncontrolled retrospective cohort studies were available, with the largest including only 43 patients. Randomized trials that

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compare CRS plus HIPEC with standard treatment (e.g., CRS alone or systemic chemotherapy alone) are needed. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have peritoneal mesothelioma who receive CRS plus HIPEC, the evidence includes retrospective cohort studies and systematic reviews. Relevant outcomes are OS, disease-specific survival, QOL, and treatment-related mortality and morbidity. Retrospective cohort studies have shown median and 5-year OS ranging from 30 to 92 months and from 33% to 68%, respectively, for patients with peritoneal mesothelioma treated with CRS plus HIPEC. Although no RCTs or comparative studies have been published, historical case series have reported a median survival of 12 months with treatment by palliative surgery, systemic or intraperitoneal chemotherapy, and abdominal irradiation. Procedure-related morbidity and mortality rates with CRS plus HIPEC have remained relatively steady over time, at approximately 35% and 5%, respectively. Because the prevalence of peritoneal mesothelioma is very low, conducting comparative trials is difficult. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have newly diagnosed stage III ovarian cancer who receive CRS plus HIPEC, the evidence includes systematic reviews and RCTs. Relevant outcomes are OS, disease-specific survival, QOL, and treatment-related mortality and morbidity. For patients with newly diagnosed stage III ovarian cancer who had received neoadjuvant chemotherapy, HIPEC increased the time to disease recurrence and reduced mortality. It did not increase serious adverse events compared with surgery alone. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have recurrent stage IIIC or IV ovarian cancer who receive CRS plus HIPEC, the evidence includes RCTs and systematic reviews. Relevant outcomes are OS, disease-specific survival, QOL, and treatment-related mortality and morbidity. For recurrent stage IIIC or IV disease (second-line setting), evidence from an RCT indicated that CRS plus HIPEC improved survival compared with CRS without HIPEC. However, interpretation of this study is limited because treatment groups in this RCT were unbalanced at baseline (variation in the completeness of cytoreduction), which has been shown to be associated with survival. Another RCT reported that CRS plus HIPEC did not result in superior outcomes compared to CRS without HIPEC for patients with platinum-sensitive recurrent disease. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have appendiceal goblet cell tumors who receive CRS plus HIPEC, the evidence includes retrospective cohort studies. Relevant outcomes are OS, disease-specific survival, QOL, and treatment-related mortality and morbidity. A propensity score-matched analysis found that CRS plus HIPEC was associated with improved median survival compared to surgery alone. However, this analysis was limited by the retrospective nature of the data and small sample size (N = 44). Rates of complete cytoreduction were not reported or accounted for in this study, so between-group differences in this or other variables may have influenced the

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observed outcomes. Additional studies are needed. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

### V. DEFINITIONS

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**CYTOREDUCTION SURGERY** involves mobilization of the liver, exploration of the diaphragm, mobilization of the stomach, exploration of the bilateral abdominal gutters, pelvic recesses, and mobilization of the large and small bowel with examination for tumor deposits along their entire length.

**INTRAPERITONEAL** refers to within the peritoneal cavity. The peritoneum is a serous membrane lining the abdominal cavity and reflected over the viscera.

### VI. BENEFIT VARIATIONS

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The existence of this medical policy does not mean that this service is a covered benefit under the member's health benefit plan. Benefit determinations should be based in all cases on the applicable health benefit plan language. Medical policies do not constitute a description of benefits. A member's health benefit plan governs which services are covered, which are excluded, which are subject to benefit limits, and which require preauthorization. There are different benefit plan designs in each product administered by Capital Blue Cross. Members and providers should consult the member's health benefit plan for information or contact Capital Blue Cross for benefit information.

### VII. DISCLAIMER

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*Capital Blue Cross's medical policies are developed to assist in administering a member's benefits, do not constitute medical advice and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy between this medical policy and a member's benefit information, the benefit information will govern. If a provider or a member has a question concerning the application of this medical policy to a specific member's plan of benefits, please contact Capital Blue Cross' Provider Services or Member Services. Capital Blue Cross considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.*

### VIII. CODING INFORMATION

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**Note:** This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.



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### Covered when medically necessary:

Procedure Codes							
96446	96547	96548	96549				

ICD-10-CM Diagnosis Codes	Description
C45.1	Mesothelioma of peritoneum
C56.1	Malignant neoplasm of right ovary
C56.2	Malignant neoplasm of left ovary
C56.3	Malignant neoplasm of bilateral ovaries
C56.9	Malignant neoplasm of unspecified ovary
C57.00	Malignant neoplasm of unspecified fallopian tube
C57.01	Malignant neoplasm of right fallopian tube
C57.02	Malignant neoplasm of left fallopian tube
C78.6	Secondary malignant neoplasm of retroperitoneum and peritoneum
C79.60	Secondary malignant neoplasm of unspecified ovary
C79.61	Secondary malignant neoplasm of right ovary
C79.62	Secondary malignant neoplasm of left ovary
C79.63	Secondary malignant neoplasm of bilateral ovaries
D12.1	Benign neoplasm of appendix

## IX. REFERENCES

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1. *Maggiore L, Elias D. Curative treatment of colorectal peritoneal carcinomatosis: current status and future trends. Eur J Surg Oncol. Jul 2010; 36(7): 599-603. PMID 20605396*
2. *National Organization for Rare Disorders. Pseudomyxoma peritonei*
3. *Elias D, Honore C, Ciuchendea R, et al. Peritoneal pseudomyxoma: results of a systematic policy of complete cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. Br J Surg. Sep 2008; 95(9): 1164-71. PMID 18690633*
4. *Yonemura Y, Kawamura T, Bandou E, et al. Advances in the management of gastric cancer with peritoneal dissemination. Recent Results Cancer Res. 2007; 169: 157-64. PMID 17506258*
5. *Yonemura Y, Endou Y, Shinbo M, et al. Safety and efficacy of bidirectional chemotherapy for treatment of patients with peritoneal dissemination from gastric cancer: Selection for cytoreductive surgery. J Surg Oncol. Sep 15, 2009; 100(4): 311-6. PMID 19697437*
6. *National Comprehensive Cancer Network (NCCN). NCCN Clinical practice guidelines in oncology: gastric cancer. Version 1.2023*
7. *Baratti D, Kusamura S, Deraco M. Diffuse malignant peritoneal mesothelioma: systematic review of clinical management and biological research. J Surg Oncol. Jun 2011; 103(8): 822-31. PMID 21283990*

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8. Chornokur G, Amankwah EK, Schildkraut JM, et al. Global ovarian cancer health disparities. *Gynecol Oncol.* Apr 2013; 129(1): 258-64. PMID 23266352
9. Glockzin G, Ghali N, Lang SA, et al. Results of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for peritoneal carcinomatosis from colorectal cancer. *J Surg Oncol.* Sep 15, 2009; 100(4): 306-10. PMID 19697436
10. Jimenez W, Sardi A, Nieroda C, et al. Predictive and prognostic survival factors in peritoneal carcinomatosis from appendiceal cancer after cytoreductive surgery with hyperthermic intraperitoneal chemotherapy. *Ann Surg Oncol.* Dec 2014; 21(13): 4218-25. PMID 24986239
11. Glehen O, Gilly FN, Boutitie F, et al. Toward curative treatment of peritoneal carcinomatosis from nonovarian origin by cytoreductive surgery combined with perioperative intraperitoneal chemotherapy: a multi-institutional study of 1,290 patients. *Cancer.* Dec 15, 2010; 116(24): 5608-18. PMID 20737573
12. Elias D, Gilly F, Quenet F, et al. Pseudomyxoma peritonei: a French multicentric study of 301 patients treated with cytoreductive surgery and intraperitoneal chemotherapy. *Eur J Surg Oncol.* May 2010; 36(5): 456-62. PMID 20227231
13. Chua TC, Yan TD, Smigielski ME, et al. Long-term survival in patients with pseudomyxoma peritonei treated with cytoreductive surgery and perioperative intraperitoneal chemotherapy: 10 years of experience from a single institution. *Ann Surg Oncol.* Jul 2009; 16(7): 1903-11. PMID 19387742
14. Vaira M, Cioppa T, DE Marco G, et al. Management of pseudomyxoma peritonei by cytoreduction+HIPEC (hyperthermic intraperitoneal chemotherapy): results analysis of a twelve-year experience. *In Vivo.* Jul-Aug 2009; 23(4): 639-44. PMID 19567401
15. Marcotte E, Dube P, Drolet P, et al. Hyperthermic intraperitoneal chemotherapy with oxaliplatin as treatment for peritoneal carcinomatosis arising from the appendix and pseudomyxoma peritonei: a survival analysis. *World J Surg Oncol.* Nov 07, 2014; 12: 332. PMID 25380618
16. Yan TD, Black D, Savady R, et al. A systematic review on the efficacy of cytoreductive surgery and perioperative intraperitoneal chemotherapy for pseudomyxoma peritonei. *Ann Surg Oncol.* Feb 2007; 14(2): 484-92. PMID 17054002
17. Lord AC, Shihab O, Chandrakumaran K, et al. Recurrence and outcome after complete tumour removal and hyperthermic intraperitoneal chemotherapy in 512 patients with pseudomyxoma peritonei from perforated appendiceal mucinous tumours. *Eur J Surg Oncol.* Mar 2015; 41(3): 396-9. PMID 25216980
18. Sardi A, Jimenez WA, Nieroda C, et al. Repeated cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in peritoneal carcinomatosis from appendiceal cancer: analysis of survival outcomes. *Eur J Surg Oncol.* Nov 2013; 39(11): 1207-13. PMID 24007834
19. Li J, Wang AR, Chen XD, et al. Effect of hyperthermic intraperitoneal chemotherapy in combination with cytoreductive surgery on the prognosis of patients with colorectal cancer peritoneal metastasis: a systematic review and meta-analysis. *World J Surg Oncol.* Jun 14 2022; 20(1): 200. PMID 35701802
20. Huang CQ, Min Y, Wang SY, et al. Cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy improves survival for peritoneal carcinomatosis from colorectal cancer: a systematic review and meta-analysis of current evidence. *Oncotarget.* Aug 15, 2017; 8(33): 55657-55683. PMID 28903452

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21. Shan LL, Saxena A, Shan BL, et al. Quality of life after cytoreductive surgery and hyperthermic intra-peritoneal chemotherapy for peritoneal carcinomatosis: A systematic review and meta-analysis. *Surg Oncol.* Dec 2014; 23(4): 199-210. PMID 25466850
22. Seretis C, Youssef H. Quality of life after cytoreductive surgery and intraoperative hyperthermic intraperitoneal chemotherapy for peritoneal surface malignancies: a systematic review. *Eur J Surg Oncol.* Dec 2014; 40(12): 1605-13. PMID 25242382
23. Quenet F, Elias D, Roca L, et al. Cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy versus cytoreductive surgery alone for colorectal peritoneal metastases (PRODIGE 7): a multicentre, randomised, open-label, phase 3 trial. *Lancet Oncol.* Feb 2021; 22(2): 256-266. PMID 33476595
24. Verwaal VJ, van Ruth S, de Bree E, et al. Randomized trial of cytoreduction and hyperthermic intraperitoneal chemotherapy versus systemic chemotherapy and palliative surgery in patients with peritoneal carcinomatosis of colorectal cancer. *J Clin Oncol.* Oct 15, 2003; 21(20): 3737-43. PMID 14551293
25. Verwaal VJ, Bruin S, Boot H, et al. 8-year follow-up of randomized trial: cytoreduction and hyperthermic intraperitoneal chemotherapy versus systemic chemotherapy in patients with peritoneal carcinomatosis of colorectal cancer. *Ann Surg Oncol.* Sep 2008; 15(9): 2426-32. PMID 18521686
26. Granieri S, Bonomi A, Frassini S, et al. Prognostic impact of cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) in gastric cancer patients: A meta-analysis of randomized controlled trials. *Eur J Surg Oncol.* Nov 2021; 47(11): 2757-2767. PMID 34001385
27. Desiderio J, Chao J, Melstrom L, et al. The 30-year experience-A meta-analysis of randomised and high-quality non-randomised studies of hyperthermic intraperitoneal chemotherapy in the treatment of gastric cancer. *Eur J Cancer.* Jul 2017; 79: 1-14. PMID 28456089
28. Rudloff U, Langan RC, Mullinax JE, et al. Impact of maximal cytoreductive surgery plus regional heated intraperitoneal chemotherapy (HIPEC) on outcome of patients with peritoneal carcinomatosis of gastric origin: results of the GYMSSA trial. *J Surg Oncol.* Sep 2014; 110(3): 275-84. PMID 25042700
29. Yang XJ, Huang CQ, Suo T, et al. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy improves survival of patients with peritoneal carcinomatosis from gastric cancer: final results of a phase III randomized clinical trial. *Ann Surg Oncol.* Jun 2011; 18(6): 1575-81. PMID 21431408
30. Navarro-Barrios A, Gil-Martinez J, Ramos-Bernardo I, et al. Intraperitoneal hyperthermic chemotherapy after cytoreduction in patients with peritoneal metastases from endometrial cancer. The next frontier? *Surg Oncol.* Jun 2020; 33: 19-23. PMID 32561085
31. Cornali T, Sammartino P, Kopanakis N, et al. Cytoreductive Surgery Plus Hyperthermic Intraperitoneal Chemotherapy for Patients with Peritoneal Metastases from Endometrial Cancer. *Ann Surg Oncol.* Mar 2018; 25(3): 679-687. PMID 29282600
32. Helm JH, Miura JT, Glenn JA, et al. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for malignant peritoneal mesothelioma: a systematic review and meta-analysis. *Ann Surg Oncol.* May 2015; 22(5): 1686-93. PMID 25124472

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<b>POLICY NUMBER</b>	<b>MP-2.021</b>

33. Robella M, Vaira M, Mellano A, et al. Treatment of diffuse malignant peritoneal mesothelioma (DMPM) by cytoreductive surgery and HIPEC. *Minerva Chir.* Feb 2014; 69(1): 9-15. PMID 24675242
34. Alexander HR, Bartlett DL, Pingpank JF, et al. Treatment factors associated with long-term survival after cytoreductive surgery and regional chemotherapy for patients with malignant peritoneal mesothelioma. *Surgery.* Jun 2013; 153(6): 779-86. PMID 23489943
35. Yan TD, Deraco M, Baratti D, et al. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for malignant peritoneal mesothelioma: multi-institutional experience. *J Clin Oncol.* Dec 20, 2009; 27(36): 6237-42. PMID 19917862
36. Kim SI, Kim JH, Lee S, et al. Hyperthermic intraperitoneal chemotherapy for epithelial ovarian cancer: A meta-analysis. *Gynecol Oncol.* Dec 2022; 167(3): 547-556. PMID 36273925
37. Zhang G, Zhu Y, Liu C, et al. The prognosis impact of hyperthermic intraperitoneal chemotherapy (HIPEC) plus cytoreductive surgery (CRS) in advanced ovarian cancer: the meta-analysis. *J Ovarian Res.* Apr 17, 2019; 12(1): 33. PMID 30995948
38. Wang Y, Ren F, Chen P, et al. Effects of CytoReductive surgery plus hyperthermic IntraPERitoneal chemotherapy (HIPEC) versus CytoReductive surgery for ovarian cancer patients: A systematic review and meta-analysis. *Eur J Surg Oncol.* Mar 2019; 45(3): 301-309. PMID 30786961
39. Antonio CCP, Alida GG, Elena GG, et al. Cytoreductive Surgery With or Without HIPEC After Neoadjuvant Chemotherapy in Ovarian Cancer: A Phase 3 Clinical Trial. *Ann Surg Oncol.* Apr 2022; 29(4): 2617-2625. PMID 34812982
40. van Driel WJ, Koole SN, Sikorska K, et al. Hyperthermic Intraperitoneal Chemotherapy in Ovarian Cancer. *N Engl J Med.* Jan 18, 2018; 378(3): 230-240. PMID 29342393
41. Huo YR, Richards A, Liauw W, et al. Hyperthermic intraperitoneal chemotherapy (HIPEC) and cytoreductive surgery (CRS) in ovarian cancer: A systematic review and meta-analysis. *Eur J Surg Oncol.* Dec 2015; 41(12): 1578-89. PMID 26453145
42. Spiliotis J, Halkia E, Lianos E, et al. Cytoreductive surgery and HIPEC in recurrent epithelial ovarian cancer: a prospective randomized phase III study. *Ann Surg Oncol.* May 2015; 22(5): 1570-5. PMID 25391263
43. Zivanovic O, Chi DS, Zhou Q, et al. Secondary Cytoreduction and Carboplatin Hyperthermic Intraperitoneal Chemotherapy for Platinum-Sensitive Recurrent Ovarian Cancer: An MSK Team Ovary Phase II Study. *J Clin Oncol.* Aug 10, 2021; 39(23): 2594-2604. PMID 34019431
44. Sluiter NR, van der Bilt JD, Croll DMR, et al. Cytoreduction and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) Versus Surgery Without HIPEC for Goblet-Cell Carcinoids and Mixed Adenoneuroendocrine Carcinomas: Propensity Score-Matched Analysis of Centers in the Netherlands and Belgium. *Clin Colorectal Cancer.* Sep 2020; 19(3): e87-e99. PMID 32651131
45. McConnell YJ, Mack LA, Gui X, et al. Cytoreductive surgery with hyperthermic intraperitoneal chemotherapy: an emerging treatment option for advanced goblet cell tumors of the appendix. *Ann Surg Oncol.* Jun 2014; 21(6): 1975-82. PMID 24398544
46. Zambrano-Vera K, Sardi A, Munoz-Zuluaga C, et al. Outcomes in Peritoneal Carcinomatosis from Appendiceal Goblet Cell Carcinoma Treated with Cytoreductive Surgery and

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- Hyperthermic Intraperitoneal Chemotherapy (CRS/HIPEC). Ann Surg Oncol. Jan 2020; 27(1): 179-187. PMID 31646450*
47. Morris VK, Kennedy EB, Baxter NN, et al. Treatment of Metastatic Colorectal Cancer: ASCO Guideline. *J Clin Oncol. Jan 20 2023; 41(3): 678-700. PMID 36252154*
  48. Vogel JD, Felder SI, Bhama AR, et al. The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for the Management of Colon Cancer. *Dis Colon Rectum. Feb 01, 2022; 65(2): 148-177. PMID 34775402*
  49. Glasgow SC, Gaertner W, Stewart D, et al. The American Society of Colon and Rectal Surgeons, Clinical Practice Guidelines for the Management of Appendiceal Neoplasms. *Dis Colon Rectum. Dec 2019; 62(12): 1425-1438. PMID 31725580*
  50. National Comprehensive Cancer Network (NCCN). NCCN Clinical practice guidelines in oncology: colon cancer. Version 2.2023
  51. National Comprehensive Cancer Network (NCCN). NCCN Clinical practice guidelines in oncology: uterine neoplasms. Version 2.2023
  52. National Comprehensive Cancer Network (NCCN). NCCN Clinical practice guidelines in oncology: rectal cancer. Version 2.2023
  53. National Comprehensive Cancer Network (NCCN). NCCN Clinical practice guidelines in oncology: ovarian cancer including fallopian tube cancer and primary peritoneal cancer. Version 1.2023
  54. Hoppenot C, Schuitevoerder D, Izquierdo FJ, et al. The Chicago Consensus on Peritoneal Surface Malignancies: Management of Ovarian Neoplasms. *Ann Surg Oncol. Jun 2020; 27(6): 1780-1787. PMID 32285271*
  55. Izquierdo FJ, Schuitevoerder D, Plana A, et al. The Chicago Consensus on Peritoneal Surface Malignancies: Management of Colorectal Metastases. *Ann Surg Oncol. Jun 2020; 27(6): 1761-1767. PMID 32285270*
  56. Izquierdo FJ, Schuitevoerder D, Plana A, et al. The Chicago Consensus on Peritoneal Surface Malignancies: Management of Gastric Metastases. *Ann Surg Oncol. Jun 2020; 27(6): 1768-1773. PMID 32285269*
  57. Schuitevoerder D, Izquierdo FJ, Plana A, et al. The Chicago Consensus on Peritoneal Surface Malignancies: Management of Peritoneal Mesothelioma. *Ann Surg Oncol. Jun 2020; 27(6): 1774-1779. PMID 32285273*
  58. Schuitevoerder D, Plana A, Izquierdo FJ, et al. The Chicago Consensus on Peritoneal Surface Malignancies: Management of Appendiceal Neoplasms. *Ann Surg Oncol. Jun 2020; 27(6): 1753-1760. PMID 32285275*
  58. Blue Cross Blue Shield Association Medical Policy Reference Manual. 2.03.07, Hyperthermic Intraperitoneal Chemotherapy for Select Intra-Abdominal and Pelvic Malignancies. August 2023

### X. POLICY HISTORY

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<b>MP 2.021</b>	<b>CAC 3/25/03</b>
	<b>CAC 3/29/05</b>
	<b>CAC 11/29/05</b>
	<b>CAC 11/28/06</b>
	<b>CAC 11/27/07</b>

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<b>CAC 11/25/08</b>
<b>CAC 9/29/09</b> Consensus Review
<b>CAC 1/25/11</b> Adopt BCBSA. Revised title to Hyperthermia for Cancer Therapy/Cytoreduction and Hyperthermic Intraperitoneal Chemotherapy. Cytoreduction and hyperthermic intraperitoneal chemotherapy was changed from investigational to medically necessary for the treatment of pseudomyxoma peronei. Added statement indicating cytoreduction and hyperthermic intraperitoneal chemotherapy for peritoneal carcinomatosis from colon cancer is investigational.
<b>CAC 6/26/12.</b> Minor revision Policy statement added that cytoreductive surgery and perioperative intraperitoneal chemotherapy for the treatment of peritoneal mesothelioma may be considered medically necessary. Title changed to include peritoneal mesothelioma. Use of the term “hyperthermic” changed to “perioperative” in the title and policy statements to include early postoperative intraperitoneal chemotherapy. Use of the term “cytoreduction” changed to “cytoreductive surgery” to be more specific. Criteria related to local and whole-body hyperthermia removed from policy. <b>7/9/12</b> FEP variation added.
<b>CAC 9/24/13 Consensus review.</b> References updated but no changes to the policy statements. Administrative code review complete.
<b>CAC 7/22/14 Consensus review.</b> No change to policy statement. References updated. Rationale section added. Removed Medicare variation to NCD 110.1 – information related to hyperthermia was removed from this policy at previous review.
<b>CAC 7/21/15 Minor revision.</b> Investigational policy statement added for ovarian cancer, peritoneal carcinomatosis due to gastric or endometrial cancer and for all other indications. Medically necessary policy statement unchanged. Title changed to “Cytoreductive Surgery and Perioperative Intraperitoneal Chemotherapy for Select Intra-Abdominal and Pelvic Malignancies”. Background, rationale, and references updated. Codes reviewed.
<b>Administrative Update 12/1/16.</b> Variation section reformatted.
<b>CAC 3/28/17 Consensus review.</b> No change to the policy statements. Description/Background, Regulatory Status, Rationale and Reference sections updated. Coding reviewed.
<b>1/2/18 Consensus review.</b> No changes to the policy statements. Background, rationale, and references updated.
<b>12/3/18 Minor review.</b> Changed hyperthermic intraperitoneal chemotherapy for the treatment of newly diagnosed stage III ovarian cancer from investigational to medically necessary. Policy title changed to “Hyperthermic Intraperitoneal Chemotherapy for Select Intra-Abdominal and Pelvic Malignancies.”
<b>11/18/19 Consensus review.</b> No changes to the policy statement. Coding reviewed; diagnosis codes added. References updated. Effective 3/1/2020.
<b>9/4/20 Consensus review.</b> No changes to policy statement. References unchanged, coding reviewed.

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<b>6/4/2021 Consensus review.</b> No change to policy statement. References, background, and rationale updated. Coding reviewed. Added NCCN statement
<b>9/7/2021 Administrative update.</b> New codes C56.3 and C79.63 added. Effective 10/1/2021
<b>10/17/2022 Consensus Review.</b> No change to policy statement. Background, rationale, and references updated. Coding reviewed
<b>08/09/2023 Consensus Review.</b> No change to policy statement. Product variation language, Background and References updated.
<b>12/12/2023 Admin Update:</b> Added New Codes 96547 & 96548. Effective 1/1/24.

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